Frequency of coincident iron deficiency and β -thalassaemia trait in British Asian children

R F Hinchliffe, J S Lilleyman

Abstract

A study was carried out to determine the frequency of combined iron deficiency and β -thalassaemia trait in a cohort of British Asian children to see whether the trait protects iron status. Of 470 consecutive children with red cell microcytosis, 77 had β -thalassaemia trait and 26 (34%) of these also had evidence of iron deficiency. It was most common and profound in children under five years of age where the prevalence was 16 in 33 (48.5%). This suggests that iron deficiency is no less common in Asian children with β -thalassaemia trait than in those without. It should not be presumed that the trait protects iron status or that the two are in any way mutually exclusive, at least in the early years.

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Although iron deficiency and β -thalassaemia trait are both common in the British Asian population,¹ there is uncertainty about the frequency of their co-existence. It has been suggested that the trait confers an advantage in maintaining iron balance,²⁻⁴ in which case the prevalence of iron deficiency should be lower in those with this trait.

To find out whether that suggestion applies in childhood, we examined a consecutive cohort of children with the trait to see how many also showed features of iron deficiency. We then attempted to assess whether that proportion differed from iron deficient British Asian children who did not have the trait.

Methods

Over a six year period, referring clinicians were asked to provide venous samples from all children of South Asian ethnic origin over six months old who had had a skin puncture blood count and whose red cells had been found to be microcytic. Where obtained, this further sample was used to perform haemoglobin (Hb)

electrophoresis and quantitation of HbA₂, HbF and plasma ferritin concentrations. During the latter half of the study, red cell zinc protoporphyrin (ZPP) was also measured using a ZPP meter (Helena Laboratories, Gateshead, UK). Children were considered to have β -thalassaemia trait if the concentration of HbA₂ was $\geq 4\%$, and to have iron deficiency if the plasma ferritin concentration was $<12 \mu\text{g/l}$ and/or red cell ZPP was $>75 \mu\text{mol/mol haem}$. In children with the trait an upper limit for ZPP was defined as $139 \mu\text{mol ZPP/mol haem}$, this being the mean + 2SD value obtained from the results of those who were considered to be iron replete (haemoglobin $\geq 100 \text{ g/l}$, mean cell haemoglobin (MCH) $\geq 18 \text{ pg}$, ferritin $\geq 12 \mu\text{g/l}$). Results were analysed in three age groups: 0.5-4.9 years, 5.0-9.9 years and ≥ 10 years.

Results

Of 2889 children of South Asian origin seen in the six years 1987-1992, 901 (31.2%) were found to be microcytic for their age. Further investigation was possible in 470, and 77 were found to have β -thalassaemia trait. Twenty six (34%) of these also had iron deficiency. This was more frequent (16 of 33; 48.5%) and more often clinically important in those under five years of age. In older children it was mainly restricted to a reduction in iron stores alone, with little or no additional anaemia and no change in mean corpuscular volume (MCV) or MCH concentrations. Haemoglobin A₂ concentrations in those who were iron deficient were not significantly different from those who were not (table). There was no significant correlation between HbA₂ values and either total haemoglobin, ferritin or ZPP concentrations in children with β -thalassaemia trait as a whole or in those with iron deficiency.

Estimation of the incidence of clinical iron deficiency in children under five without the trait was made based on the calculated overall proportion of such children showing microcytosis and iron deficiency with a normal HbA₂ concentration. In this way a figure of 29.8% was derived.

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Haematological variables (mean (SD)) in children with β -thalassaemia trait grouped according to age and iron status

Age (years)	Iron status	No. of cases	Haemoglobin (g/l)	MCV (fl)	MCH (pg)	HbA ₂ (%)
0.5-4.9	Replete	17	104 (11.0)	56.9 (4.1)	18.3 (1.4)	5.2 (0.9)
	Deficient	16	88 (15.0)	47.3 (7.5)	14.5 (2.5)	5.2 (0.8)
5.0-9.9	Replete	14	105 (6.0)	55.4 (3.1)	17.9 (0.9)	5.8 (1.0)
	Deficient	7	98 (10.0)	56.1 (4.2)	17.1 (1.0)	6.0 (0.4)
>10	Replete	20	107 (8.0)	57.5 (3.4)	18.2 (1.0)	5.6 (0.7)
	Deficient	3	107 (8.0)	61.7 (0.6)	19.3 (0.3)	5.8 (0.9)

Discussion

β -thalassaemia trait produces mild ineffective erythropoiesis associated with increased iron absorption. It might therefore be expected to give some degree of protection against iron deficiency, and there is evidence to support this from some studies^{2,3} but not from others.⁴ Iron deficiency is a very common problem in British Asian children,⁵ and our findings suggest that the trait does nothing to prevent it, at least in those under five years of age.

The design of this study renders comparisons of the prevalence of iron deficiency between those with and without the trait difficult. By selecting patients on the basis of microcytosis, non-trait children with simply reduced iron stores (that is, not yet microcytic) were not detected whereas those with the trait (in whom microcytosis is an almost universal finding) were. This is illustrated in our study by the blood count values of children with β -thalassaemia trait over five years of age where those with reduced iron stores had MCV and MCH values almost identical with those of their iron-replete counterparts (table). We will have therefore underestimated the frequency of reduced iron stores in non-trait children. Our calculated figure of 29.8% for the prevalence of microcytic iron deficiency in children aged under five years compares well with that of 24.5% found in a recent study of preschool Asian children in North London.⁶ The prevalence of biochemically demonstrable reduced iron stores in that study, however, as opposed to red cell changes, was much higher at 46.6%—a similar figure to our 48.5% for young children with β -thalassaemia trait. It also tallies with Ehrhardt's⁵ figure of 45.3% for the incidence

of ferritin levels $<10 \mu\text{g/l}$ in preschool Asian children in Bradford.

We therefore conclude that clinical iron deficiency occurs with a very high frequency in children under five years of age with β -thalassaemia trait and that any advantage in iron supply conferred by the trait is trivial and unimportant in this context. The combined state should always be suspected. Iron supplements are often needed irrespective of the presence of the trait. We are less able to comment on the situation in older children, as their smaller numbers do not allow reliable conclusions to be drawn, and some degree of protection of iron status cannot be excluded.

Full laboratory investigations, including estimation of HbA₂, should be carried out in all Asian toddlers with microcytic hypochromic anaemia. Concern about the reliability of HbA₂ quantitation in the presence of iron deficiency⁷ does not appear to be relevant in the clinical context in question, and the test can be used confidently as a discriminant.

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